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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,888	12/21/2001	William Canfield	203515US77	5416

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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<b>Office Action Summary</b>	<b>Application No.</b> 10/023,888	<b>Applicant(s)</b> CANFIELD ET AL.	
	<b>Examiner</b> Elizabeth Slobodyansky	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☒ This action is **FINAL**.      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22,26,28-37 and 54-95 is/are pending in the application.
- 4a) Of the above claim(s) 54,55,58-68 and 74-95 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 22 is/are allowed.
- 6) ☒ Claim(s) 26,28-37,56,57 and 70-73 is/are rejected.
- 7) ☒ Claim(s) 69 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \*   c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9/22/03.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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### **DETAILED ACTION**

The amendment filed September 22, 2003 canceling claims 1-21, 23-25, 27 and 38-53 and adding claims 56-95 has been entered.

Claims 22, 26, 28-37 and 54-95 are pending.

### ***Election/Restriction***

Claims 54 and 55 have been withdrawn as drawn to methods of use of products, lysosomal hydrolases, that are different from the claimed product, GlcNAc-phosphotransferase (Office action mailed April 22, 2003).

New claims 56-95 are directed to non-elected inventions (Remarks of September 22, 2003, page 11). Claims 56, 57 and 69-73 are rejoined with claim 22 as drawn to a method of use of the allowed product of claim 22. Claims 58-68, 74 and 75 are not rejoined as it appears that their scope is different and unclear. Claims 76-95 are not rejoined as dependent from non-allowed product of claim 26.

Claims 22, 26, 28-37, 56, 57 and 69-73 are under consideration.

### ***Claim Objections***

Claim 26, with dependent claims 28-37, and claim 70 are objected to because of the following informalities:

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Claim 26 recites abbreviation "GlcNAc phosphotransferase". It is suggested that the first time an abbreviation is used in a claim, that the abbreviated term be written out in full, followed by its abbreviation in parenthesis.

Claim 70 recites "G<sub>M1</sub> Galglioside" where it appears "G<sub>M1</sub> Ganglioside" is intended.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26 and 28-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 26 and 28-37 are directed to an GlcNAc-phosphotransferase comprising  $\alpha$  and  $\beta$  subunits and not endogenous proteolytic cleavage site between them.

Therefore, the claims are directed to a genus of GlcNAc-phosphotransferases comprising subunits from any source both naturally occurring and man made having

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any structure. The subunits encompass polypeptides of unknown function and structure with any stoichiometry between subunits. The specification teaches the structure of only a single representative species of such GlcNAc-phosphotransferases, the GlcNAc-phosphotransferase having the amino acid sequence of SEQ ID NO:2 comprising cytosolic fragments of human GlcNAc-phosphotransferase  $\alpha$  and  $\beta$  subunits linked via the Furin proteolytic cleavage site (SEQ ID NO:24, residues 913-918 of SEQ ID NO:2). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being GlcNAc-phosphotransferase. Furthermore, with regard to  $\alpha$  and  $\beta$  subunits the specification, the specification teaches the structure of only a single representative species of each subunit having the amino acid sequences of SEQ ID NO: 4 and 5, respectively. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of being " $\alpha$  and  $\beta$  subunits" and fails to provide any structure:function correlation present in all members of the claimed genus. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

The claims reciting the specific sequence of one subunit are included in this rejection because the second subunit is not described by the specific sequence.

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Claims 56, 57 and 70-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a GlcNAc phosphotransferase of SEQ ID NO:2 for transferring N-acetylglucosamine 1-phosphate to mannose residues on lysosomal hydrolases, does not reasonably provide enablement for using a GlcNAc phosphotransferase of SEQ ID NO:2 for transferring N-acetylglucosamine 1-phosphate to mannose residues on any protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification and the art teach that phosphorylation of lysosomal hydrolases occurs in two steps comprising the first step of transferring N-acetylglucosamine 1-phosphate to mannose residues on lysosomal hydrolases by GlcNAc phosphotransferase (e.g., Baranski et al., JBC, 267, 23342-23348, 1992, form PTO-1449 filed September 22, 2003; specification, page 3, lines 15-18).

The term "phosphorylation" means adding phosphate group. It can be carbohydrate or amino acid residue. GlcNAc phosphotransferase adds phosphate group to the 6 position of 1, 2-linked mannoses on the lysosomal enzyme (specification, page 3, lines 18-20). It does not add phosphate to any other carbohydrate or amino acid residue on any protein.

Therefore, one of ordinary skill would require guidance, beyond that provided, to use GlcNAc phosphotransferase of SEQ ID NO:2 for transferring N-acetylglucosamine

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1-phosphate to mannose residues on a protein other than lysosomal hydrolase or for phosphorylating any protein. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35 and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 recites various proteolytic cleavage sites. The specification teaches that said sites are represented by SEQ ID NOs:22-25 (page 21, lines 20-22). It is known in the art that enterokinase cleaves 6-Lys--Ile-7 bond in trypsinogen. No such bond is shown in SEQ ID NO:23, which is depicted as Enterokinase cleavage site on Figure 5, or any of SEQ ID NOs: 22-25. It is known in the art that Factor Xa cleaves Arg--Thr and then Arg--Ile bonds in prothrombin to form thrombin. No such bonds are shown in SEQ ID NO:22, which is depicted as Factor Xa cleavage site on Figure 5, or any of SEQ ID NOs: 22-25.

While it is known that Furin cleaves Arg-Xaa-Arg/Lys-Arg--Yaa bonds of which SEQ ID NO:24 is representative, it is unclear which amino acid sequences other than SEQ ID NO:25 correspond to "Genease I proteolytic cleavage site".

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Claim 70 recites a lysosomal enzyme "selected from the group consisting of". Said group comprises products that are not enzymes such as, for example, "G<sub>M1</sub> Galglioside", "cerebroside", etc. Further, there are "acid  $\beta$ -galactosidase" and "acid - galactosidase" recited where it appears only one enzyme is intended. The difference between "Lysosomal sphingomyelinase" and "Sphingomyelinase" is not defined. It is unclear which enzyme is defined as "Glucocerebrosidase  $\beta$ -Glucosidase" wherein there are two different enzymes.

Claim 70 recites the limitation "enzyme" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 70 depends from claim 69 which recites "hydrolase".

### ***Allowable Subject Matter***

Claim 22 is allowed.

Claim 69 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Response to Arguments***

The 112, 1st paragraph, written description rejection of claim 22 is withdrawn because SEQ ID NO:2 is the amino acid sequence of the soluble GlcNAc



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phosphotransferase comprising  $\alpha$  and  $\beta$  subunits of human GlcNAc phosphotransferase, both subunits lacking their respective transmembrane domains, with the Furin proteolytic cleavage site (SEQ ID NO:24, residues 913-918 of SEQ ID NO:2) linking two subunits.

Applicant's arguments filed September 22, 2003 have been fully considered but they are not persuasive.

With regard to the 112, 1st paragraph, written description of claims 26, 28-37, Applicants argue that "the specification describes sequences from human, rat, and *D. melanogaster* (e.g., see SEQ ID NOS:14 and 16 in addition to SEQ ID NO:4 and 5 from human)" (Remarks, page 12, last paragraph). This is not persuasive because the claimed genus of GlcNAc-phosphotransferases comprises GlcNAc-phosphotransferases comprising subunits from any source both naturally occurring and man made having any structure and linked by any proteolytic cleavage site. The subunits encompass polypeptides of unknown function and structure with any stoichiometry between subunits.

A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative

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number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one or two species within the genus. In the instant case, even within the genus of human GlcNAc-phosphotransferases allelic and splice variants are feasible rendering the genus of human GlcNAc-phosphotransferases represented by a single polypeptide of SEQ ID NO:2, insufficiently described.

With regard to the 112, 2nd paragraph, rejection of claims 35-37, Applicants argue that "Specific examples of those proteolytic cleavage sites are depicted in Figure 5 and include the sequences of SEQ ID NOs: 22-25" (page 13). This is not persuasive for the reasons addressed above in the rejection.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

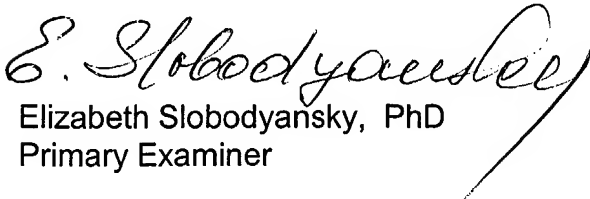
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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

  
Elizabeth Slobodyansky, PhD  
Primary Examiner

December 9, 2003